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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,898	10/03/2001	Zhiyuan Gong	1781-0163P	5940

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EXAMINER

WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/913,898

Applicant(s)

GONG ET AL.

Examiner

Joseph T. Voitach

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 March 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7-11, 13, 16 and 19-29 is/are pending in the application.
- 4a) Of the above claim(s) 22, 25, 26 and 29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7-11, 13, 16, 19-21, 23, 24, 27 and 28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 August 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

This application is a 371 national stage filing of PCT/SG99/00079, filed July 16, 1999 which claims benefit to foreign application 9900811-2, filed February 18, 1999 in Singapore.

Applicants' amendment filed March 21, 2005, has been received and entered. Claims 1-6, 12, 14, 15, 17 and 18 have been canceled. Claims 22-29 have been added. Claims 7-11, 13, 16, 19-29 are pending.

Election/Restriction

Applicant's election without traverse of group VIII in the reply filed on August 27, 2003 was acknowledged. The elected invention was a transgenic fish comprising a zebrafish fast muscle isoform of myosin light chain 2 gene promoter.

Newly added claims 23, 24, 27 and 28 are generally drawn to the elected invention, and will be examined to the extent they encompass the elected invention of a transgenic fish comprising a zebrafish fast muscle isoform of myosin light chain 2 gene promoter which is predominantly active in skeletal muscle. Newly added claims 22, 25, 26, and 29 are drawn to promoters and/or other functional expression patterns outside the elected invention, and are withdrawn from consideration.

As amended, claim 7 encompasses the use of four specific different promoters to generate four different fish which are structurally and functionally different. Again it is noted that under Rule 13.1-13.2 the allowed combinations do not include multiple products, multiple methods of using said products, and methods of making multiple products as claimed in the instant

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application, see MPEP 1850. In the instant case, Applicants claims encompass multiple inventions and do not have a special technical feature which link the inventions one to the other, and lack unity of invention. Claims 7, 10 (reciting the various specific promoters part of the original restriction requirement) , 23, and 27 (reciting activity in the muscle versus skeletal muscle) are more generic than the restricted groups directed to the specific promoters, and will be examined to the extent that it encompasses the elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 7-13, 16, 19-21, 23, 24, 27 and 28 are currently under examination as they are drawn a transgenic fish comprising a zebrafish fast muscle isoform of myosin light chain 2 gene promoter.

Claim Objections

Claims 7, 10, 16, 23 and 27 are objected to because of the reasons set forth previously for claim 10. Specifically, claim 10 was objected to because it is generic and broadly encompasses non-elected inventions. The claim should be amended to reflect the elected invention of a transgenic fish comprising a zebrafish fast muscle isoform of myosin light chain 2 gene

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promoter. Newly added claims 23 and 27 recite functional activity broader than that of the elected promoter.

Applicants indicate that they are unaware of any rule that requires amendment of the claims to reflect the elected invention, and request further clarification. See page 5, section II.

In the instant case, the Examiner is relying on the basic requirement of the restriction requirement under Rule 13.1-13.2 in which the allowed combinations do not include multiple products (MPEP 1850)(see citation in previous office action in the Election/Restriction section), and 37 CFR 1.141 which states that "Two or more independent and distinct inventions may not be claimed in one national application, except that more than one species of an invention, not to exceed a reasonable number, may be specifically claimed in different claims in one national application, provided the application also includes an allowable claim generic to all the claimed species and all the claims to species in excess of one are written in dependent form". In this case, no generic claim was initially set forth and the restriction requirement set forth four distinct inventions as they were drawn to the four specific promoters taught in the instant specification. Further, the restriction requirement set forth the inventions were structurally unique and independent of each other. The claims as now amended encompass inventions that were not elected. Applicants are required to set forth claims which are directed to one invention, in this case the elected invention.

For the reasons above and of record, the objection is maintained.

Newly added claim 24 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is

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required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In this case the elected invention and the claim language of claim 24 as it is dependent on claim 7 is one and the same. While it is accepted that generally claim 24 would limit claim 7, the scope of the elected invention encompassed by claim 7 is the same as that recited in claim 24, i.e. the embodiment and use of a zebrafish fast muscle isoform of myosin light chain 2 gene promoter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-21 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed is withdrawn.

In view of the specification as a whole, Examiner would agree that the disclosure provides support for introducing constructs into transgenic fish which produce a fluorescent protein upon expression of said construct.

Newly amended claim 16 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall

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introduce new matter into the disclosure of an application after the filing date of the application".

In this case the recitation of the specific hybridization conditions and the terminology of "providing stringency equivalent" are considered new matter. Applicants do not point to the specification for the specific support of the claim amendment. Upon review of the specification, the Examiner can find a section for "Hybridizable Variants" (page 13), however this section does not provide the specific conditions, nor what or how one determines an equivalent that would generically apply to the claimed invention.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claim 16 is also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. As noted above, the specification does not provide any clear guidance on determining the what is encompassed by the claim as amended, and would require undue experimentation because the final product to be used can not be accurately or precisely determined.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to

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include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

Claims 7-11, 13, 16, 19-21, 23, 24, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the instant case, the only zebra fish sequence (required for claim 7, 13 or 24) that is adequately described with a given function is 2.2 kb MLC2 fragment disclosed in the instant specification. Initially, a search of the art of record indicates that only one species of MLC2 exists, and there is no other specific teaching nor indication that another MLC2 exist in zebrafish. Thus, the requirement of the claims that a zebra fish MLC promoter is provided only supports one possible promoter. Additionally, to the extent that the claim is intended to encompass variants, the specification fails to provide any guidance to how modifications to the only species disclosed can be made while maintaining the required expression activity. It is noted that hybridization language is set forth in claim 16, however this insufficient to provide any functional properties to the resulting sequence. For example, a sequence of 50 base pairs

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from the 2.2 kb will hybridize, however if it does not contain the essential transcription elements for the claimed expression pattern, it will hybridize but will not be functionally for operative linkage to a transgene. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116. In the instant case, the specification provides one species, a 2.2 kb sequence of a MLC2 promoter without providing any guidance to the structure/function of this single species for use in the invention as claimed. The specification fails to provide any clear guidance to any other sequence than that specifically disclosed in the SEQ ID NO for MLC2. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998). In the instant case, Applicants have required a promoter to provide a given expression activity, however the specification fails to describe the relevant identifying characteristics of any of the nucleic acid sequences of any of the genes which can be used in the instantly claimed invention. Further,

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without a clear teaching of the essential elements of the claimed promoter the skilled artisan cannot envision all the possible variant nucleic acid sequences which would hybridize and provide the required expression pattern, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

Applicants attention is drawn to the decision of *The Regents of the University of California v. Eli Lilly and Company* (CAFC, July 1997) wherein it was stated: In claims involving chemical materials, generic formulas usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate written description of the claimed genus. In claims to genetic material, however, a generic statement such as “vertebrate insulin cDNA” or “mammalian cDNA,” without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen*). It is only a definition of a useful result rather than a definition of what it achieves as a result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming

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rejection because the specification does “little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.”).

Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. In this case, reciting a functional limitation or requiring a zebra fish promoter where evidence indicates only one species exists in nature fails to provide the necessary description of the function-structure of the claimed breadth. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In the instant case, the assertion of function and only one specific sequence isolated from nature does not provide adequate description of all the possible variants encompassed by the claims, thus the rejected claim fails to meet the written description requirement under 35 U.S.C. 112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-9, 11, 13 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Amendments to the claims and Applicants' arguments have adequately addressed the specific basis of the rejections for claims 7-9, 11, 13.

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Claim 16 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The amendment to the claim to include specific conditions is noted, however the recitation includes language of “providing stringency equivalent” without clearly setting forth what is considered an equivalent or the specific methods or means of determining this. The metes and bounds of claim 16 are indefinite because they rely on the relevant term of equivalent and what one would consider to be equivalent.

Claims 19-21 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants argue that the term is exceedingly well known in the art, citing an example of FDA guidelines, and point to the specification where such fish are recited. See Applicants amendment, page 6, section IV. Applicants’ arguments have been fully considered but not found persuasive.

Initially, the support in the specification does not appear to be for ornamental fish *per se*, and is just a general listing of applicable fish species contemplated. While it may be that some species listed may be considered ornamental, some are clearly not. Moreover, it is noted that the listing includes the recitation of “etc.” without any clear indication of the specificity of the listing. This portion of the specification fails to clearly set forth the metes and bounds of “ornamental”.

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With respect to Applicants' arguments that it would be "exceedingly well known" and the citation of FDA guidelines (which have not been provided as indicated), these arguments are not found persuasive because they rely on simply on a potential or intended use of the fish. For example, zebrafish are a common research tool. Of the other species listed in the specification such as tilapia, catfish, eel are clearly fish used in the food market. Without a clear definition of the specific species that are contemplated to be encompassed by the term "ornamental fish for the ornamental fish market" it is considered a relative term dependent solely on the intended use. Claims 19-21 are indefinite because the metes and bounds of what would be considered an "ornamental fish" is not set forth in the claims nor defined in the specification. It is unclear what specific fish are included or excluded from this term.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10, 16 and 19-21 stand and newly added claims 23, 24, 27 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Moss *et al.* (IDS reference).

Applicants argue that Moss *et al.* fails to anticipate the claimed invention because it does not teach a transgenic fish *per se*, because the transgene is transiently expressed (pages 7 and 8), it teaches the rat myosin light chain promoter (page 7) or that it will hybridize to the zebrafish promoter (page 8-claim 16), nor for the teaching of an ornamental fish. With respect to newly

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added claims Applicants note that similar arguments would apply to those present for claim 7 (page 9). See Applicants' amendment, pages 7-9. Applicants arguments have been fully considered, and found persuasive in part.

Initially, claim 7-9, 11, 13 have been removed from the basis of the rejection because it requires and encompasses a fish promoter that Moss *et al.* does not teach. However, independent claim 10 and other dependent claims have not such requirement, only the functional requirement that it is expressed selectively in skeletal muscle. As noted previously, Moss *et al.* teach a zebrafish which comprises a myosin light chain enhancer operatively linked to a sequence encoding GFP for the muscle specific expression. Characterization of the resulting fish indicated fluorescence from expression of the transgene was seen uniquely in the muscle and not other non-muscle cells in the fish. With respect to Applicants arguments that the transgenic fish of Moss *et al.* is not transgenic *per se*, as demonstrated by its transient expression, it is noted that there is no unique requirement of the pending claims regarding the expression of the transgene except for location. Moreover, a definition of transgenic animal comprises animals that comprise the transgene in all its cells as well as mosaic animals resulting from the initial methods used to generate the founder animal(s). Additionally, it is noted that there is no unique requirement that all the cells contain the transgene or express it. Further, in review of the limitations specifically recited (see claim 19 for example- that the fish be capable of breeding with other fish), clearly the independent claim must encompass a greater breadth of not having the transgene in every cell. However, more importantly, the methods for making transgenic fish in the present specification and those taught by Moss *et al.* are the same. Applicants' arguments that the teachings of Moss *et al.* fail to a transgenic fish as claimed are not persuasive because

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the claims can be reasonably interpreted to encompass mosaic transgene expression and the same methodology to generate transgenic fish are contemplated. With respect to the requirement that the fish be an ornamental fish, in view of the discussion above under 35 USC 112, second paragraph, a reasonable interpretation of the intended use and of the breadth of the claims in light of the specification would be any fish someone would want to possess. In this case the transgenic fish taught by Moss *et al.* would anticipate the claims.

Claims 7-11, 13, 16 and 19-21 rejected under 35 U.S.C. 102(b) as being anticipated by Amsterdam *et al.* (IDS reference) is withdrawn.

Amsterdam *et al.* teach a zebrafish which comprises a strong promoter operatively linked to a sequence encoding GFP for ubiquitous expression which seen throughout the embryo and resulting transgenic fish. The transgenic fish of Amsterdam *et al.* fails to anticipate the elected invention of a transgenic fish comprising a zebrafish fast muscle isoform of myosin light chain 2 gene promoter..

Conclusion

No claim is allowed.

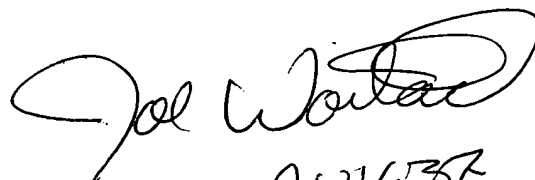
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach



Joel Woitach
AUG 30